

## **REMARKS**

Applicants respectfully request reconsideration of the rejections set forth in the Office Action mailed on September 24, 2004. All claims have been rejected. Claims 49-57, 60, 61 and 63-65 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 8, 13-15 and 52-64 of copending Application No. 09/310,879. Claims 49, 50, 54, 56, 57, 60, 61 and 63-65 have also been provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 40-43 and 51 of copending Application No. 09/718,685. Applicants are the current owner of these copending applications, and they timely file the attached terminal disclaimers in accordance with 37 C.F.R. § 1.321(c). Claims 49-57, 60, 61 and 63-66 are now pending.

### **Rejection under 35 U.S.C. § 112.**

Claims 49-57, 60, 61 and 63-66 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. More specifically, the Examiner asserted that because the claims encompass composite descriptors, which combine features derived from different cell types, and because the instant specification has allegedly failed to teach a single descriptor that includes information from different cell types, the claims have not been sufficiently described. Applicants respectfully traverse.

As a threshold matter, describing the functions of a software program is sufficient to meet the written description requirement of 35 U.S.C. § 112. See, e.g., *Robotic Vision Sys., Inc. v. View Eng'g, Inc.*, 42 U.S.P.Q. 2d 1619, 1622-23 (Fed. Cir. 1997).

Because Applicants presented this argument in detail in their Response to Office Action mailed May 10, 2004, they will not elaborate here.

Applicants first respectfully assert that the definition of “descriptors” in the specification is not as narrow as it was apparently understood by the Office. The instant specification stated that descriptors “can be formed by combining features of two or more cell components as identified using the markers.” See, e.g., page 3, line 7. Contrary to the Office’s impression that the descriptors can only be formed from features originating from the same cell lines, this definition did not limit the source of these features. Indeed, this description embraces descriptors that combine features from either the same type of cells or different types of cells.

Furthermore, in Applicants’ last amendment to the specification on August 9, 2004, Applicants properly incorporated the passage “[i]n some embodiments, the descriptors include features from different cell portions or cell types.” See page 12, line 27. While the Examiner correctly interpreted the passage to mean that a group of descriptors may include information derived from different cell types, this interpretation is by no means complete. Read in its entirety, this passage takes account of not only the situation where multiple descriptors include information derived from different cell types, but also the situation where a single descriptor includes information derived from different cell types.

Applicants next assert that explicit support is found in multiple places within the specification for “features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors.” The instant specification illustrates the relationship among “markers,” “features” and “descriptors” this way:

“[d]escriptors can be formed by combining features of 2 or more cell components as identified using the markers.” See page 3, line 8-9. Stated differently, cell features like cell components and morphological characters can be identified using the markers, and the markers can then be combined to make descriptors.

On page 24, line 17-19, a descriptor (or a fingerprint) is described as “[a] vector of two or more ... scalar values extracted from **a plurality of cell lines** and markers grown in the same condition,” whereas “scalar values” are extracted from fluorescence images (i.e., the markers) taken from cell populations. (*Emphasis added*). Therefore, any one descriptor may include information extracted from markers, which in turn identify features from multiple cell lines. Furthermore, on page 28, lines 1-6, “descriptors” were built by “quantifying and/or qualifying patterns of each marker in the **cell lines** under study” (*emphasis added*), and such studies were performed by “growing **multiple cell lines** in the presence of multiple compounds, or substances.” (*Emphasis added*). Likewise, from page 18, line 28, to page 19, line 4, Applicants describes making “**one** or more types of numerical descriptors” from values obtained from regional “fluorescence patterns of markers in **multiple cell lines** in the presence and absence of compounds.” (*Emphasis added*). Such “regional” patterns can include “determining one or more regions from around nuclei, individual cells, organelles, and the like.”

The instant specification thus adequately supports the claims. Applicants hereby respectfully request the Examiner to withdraw his rejection under 35 U.S.C. § 112, first paragraph.

Applicants thank the Examiner for withdrawing the rejection under 35 U.S.C. § 112, first paragraph.

### **Rejections under 35 U.S.C. § 103**

#### **1. Claims 49-57, 60, 61 and 63-65**

Claims 49-57, 60, 61, and 63-65 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Pauwels *et al* in view of Paull *et al*. Specifically, the Examiner acquiesced in Applicants' argument that Pauwels *et al* did not alone suggest or render obvious the instant claims because it "does not show descriptors or fingerprints that comprise information of a plurality of cell lines." See page 6, lines 5-6 of Office Action, dated September 24, 2004; see *also* page 4, paragraph 10 of Office Action, dated May 10, 2004; page 8, lines 3-7 of Amendment G, filed April 6, 2004. However, the Examiner stated that Pauwels *et al* described using digital images of treated cells to differentiate the effect of antitumor drugs on tumor cell lines, and that Paull *et al* depicted a computer program called COMPARE that clusters antitumor drugs by profiling growth inhibition of 60 tumor cells. The Examiner expressed concern that at the time of the invention, a person of ordinary skills would find it obvious to write a computer program according to Pauwels *et al*, and then modify it in order to fingerprint drugs according to Paull *et al*. Applicants respectfully disagree.

#### **No Motive to Combine – Teaching Away**

A proper obviousness rejection under 35 U.S.C. § 103(a) requires the Examiner to establish *prima facie* with evidence or reason that, at the time of the invention, (1) the prior art of record would have suggested or motivated one of ordinary skill in the art to

carry out the combination and modification of the prior art as suggested by the Examiner to arrive at the claimed invention; and (2) the prior art would have revealed that in doing so, those of ordinary skills in the art would have a reasonable expectation of success. See *In re Piasecki*, 745 F. 2d 1468, 1472 (Fed. Cir. 1984). Both the suggestion or motivation and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 20 U.S.P.Q. 2d 1438, 1442 (Fed. Cir. 1991). Motivation may be lacking when the state of the art at the time pointed researchers in a different direction than the one undertaken by the inventor. *In re Hedges*, 783 F. 2d 1038, 1041 (Fed. Cir. 1986); *Gore v. Garlock*, 721 F. 2d 1540, 1552 (Fed. Cir. 1983). Indeed, the Federal Circuit has repeatedly recognized that proceeding contrary to the accepted wisdom in the art represents strong evidence of non-obviousness. *Id.*

An explicit statement in the prior art reference that certain modification does not work certainly constitutes “teaching away.” It would also remove any reasonable expectation that such a modification would lead to likely success. Here, Pauwels *et al* failed to suggest that writing a computer program according to Paull *et al* would lead to successful prediction of drug-target interaction. In fact, Pauwels *et al* teaches away from making such a modification.

As the Examiner has pointed out, Paull *et al* described using COMPARE to analyze the inhibitory effect of antitumor drugs on the growth of tumor cell lines. Pauwels *et al*, which was published many years after Paull *et al*, attempted to use a single-variant approach just like the one taught by Paull *et al*, and found that it “do[es] not enable the pharmacological classes of the drugs to be distinguished one from another” and that “it was necessary to combine the information on the 15 parameters

into one calculation step ....” See Pauwels *et al*, page 109, lines 10-15. The result of an experiment similar to the one reported by Paull *et al* was listed on page 108 in Figure 1. According to this figure, different classes of drugs often inhibited cell proliferation or growth to the same extent among the three typical tumor cell lines, MXT, J82, and T24. From this set of cell-proliferation data, the authors were only able to conclude that aside from the drug CPA, (which had shown no cytotoxic effect), “all the other drugs had significant cytotoxic effect on cell proliferation.” See Pauwels *et al*, page 108, lines 10-13.

The MXT CELL LINE profile further illustrates this point. According Table 1 (page 106), the drug Cisplatin (CDDP) belongs to class ALK, 5-Fluorouracile (5-FU) and 6-Mercaptopurine (MP) belong to class AM, and Doxorubicin (DOX) belongs to class NDID, but their proliferation profiles are remarkably similar if not identical when it comes to their inhibitory effect on the growth of the MXT cell line. One can find numerous other examples upon a close look at Figure 1 where drugs from different pharmacological classes exert the same effect on a cell line when it comes to growth inhibition. Accordingly, Pauwels *et al* sensibly cautioned persons skilled in the art to avoid the single-parameter method taught by Paull *et al* if the goal is to distinguish cell-drug interaction. See Pauwels *et al*, page 109, lines 10-15.

Even Paull *et al* admitted that using its reported method, drugs from different classes would often rank higher than those from the same classes or are otherwise more closely related. See Paull *et al*, page 1092, lines 2-6. Therefore persons skilled in the art, after reading Pauwels *et al*, will not turn to Paull *et al* in light of the uncertain if

not dubious results obtained by Paull *et al.* The instant claims are thus not obvious under 35 U.S.C. § 103(a) over Pauwels *et al* in view of Paull *et al.*

2. Claims 63 and 66.

Claims 63 and 66 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Pauwels *et al* in view of Paull *et al*, and further in view of Rojanasakul. Initially, Applicants would like to clarify for the Examiner that claim 63 is not currently directed to antisense oligonucleotides. The obviousness rejection in view of Rojanasakul was therefore improperly imposed upon claim 63.

Further, according to the Examiner, Rojanasakul suggested that antisense oligonucleotides could be used to modulate gene expression and were potentially useful for disease therapies. The Examiner expressed concern that such a use would suggest to a person skilled in the art to modify the computer program taught by Pauwels *et al.* Applicants respectfully disagree because nowhere in Rojanasakul, Pauwels *et al*, or Paull *et al* did the authors suggest using antisense oligonucleotides to make descriptors as they are instantly claimed. Nor was there any indication of likelihood of success in using these nucleotides to differentiate drug-cell interactions.

Indeed, the only place where any suggestion to combine antisense oligonucleotides and descriptors could be found is in the instant specification. But according to the well-settled law and the MPEP, it is improper for the Examiner to look for suggestions or expectations of success from applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991); see also *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed. Cir. 1988) (stating that it would be improper to "[use] that which the inventor taught against its teacher."); MPEP, § 2143. Therefore, the deficiencies of Pauwels *et*

*a/* in view of Paull *et al/* were not rectified by Rohanasakul. Applicants accordingly request that the Examiner withdraws his rejection under 35 U.S.C. § 103(a).

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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